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## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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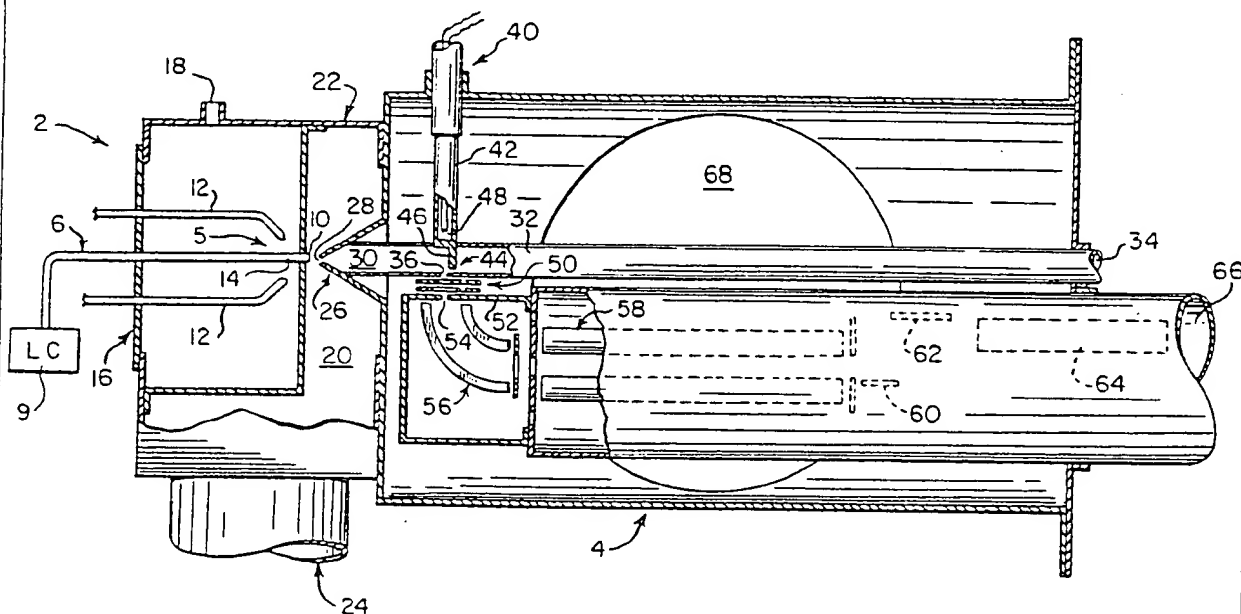
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(54) Title: ION VAPOR SOURCE FOR MASS SPECTROMETRY OF LIQUIDS



## (57) Abstract

A process for generating an ion vapor from a liquid sample can be used in interfacing a liquid chromatograph (9) to a mass spectrometer (4). The process includes generating an aerosol from the liquid. Preferably at least a fraction of the particles in the aerosol are charged. The process includes impacting the particles against a surface (46) which is maintained at a temperature above an impact-vaporization temperature. Upon colliding with the surface the particles are vaporized and an ion vapor formed.

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DescriptionIon Vapor Source for  
Mass Spectrometry of Liquids

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Government Support

The invention described herein was made in the course of work under a grant or award from the Department of Health, Education, and Welfare.

10

Technical Field

The present invention relates to the field of mass spectrometry. More particularly, the invention relates to a method and apparatus for generating an ion vapor from a liquid sample for analysis by a mass analyzer such as a quadrupole mass spectrometer. The invention is especially suited to interface a liquid chromatograph to a mass spectrometer.

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Background Art

The information in the mass spectrum of a chemical compound is of great value to chemists in identifying the compound and in characterizing its molecular structure. For those compounds for which mass spectra can be obtained, the mass spectrum typically reveals the molecular weight of the compound and the masses of a characteristic assortment of ionic fragments derived from the compound. To generate mass spectra, conventional mass spectrometers operate on a beam of ions derived from the material to be analyzed, either by deflecting the beam electromagnetically in a way which depends upon the ratio of the mass to the charge of

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the ions in the beam, or by measuring transit times of ions in a pulsed ion beam. Compounds which are to be mass analyzed generally must be converted into an ion vapor  
5 before introduction into the section of a conventional mass spectrometer which forms the ion beam.

The need to convert materials to be mass analyzed into an ion vapor has been a source of problems in the  
10 field of mass spectrometry for which no completely satisfactory solution has heretofore existed. Gaseous compounds or compounds which can be thermally vaporized without decomposition can usually be converted to an ion vapor relatively easily by heating the compound to  
15 vaporize it if it is not a gas, and either bombarding the compound in the gaseous state with a beam of electrons (electron impact ionization) or by introducing chemically-reactive ions into the gas (chemical ionization). However, many compounds are not sufficiently volatile at ambient  
20 temperatures to form a gas suitable for either electron-impact ionization or chemical ionization, and, moreover, decompose when heated so that they cannot be vaporized thermally. Among the compounds which cannot be converted into an ion vapor by these conventional techniques are  
25 many which are of biological, medical and pharmaceutical interest.

A number of special techniques have been developed to generate an ion vapor from compounds of low  
30 volatility. These techniques include field desorption, laser-assisted field desorption, plasma desorption, rapid evaporation from inert surfaces, and secondary ionization mass spectrometry. Literature citations to these and other techniques may be found in Analytical Chemistry, vol 51,  
35 pp. 682A-701A (June 1979). None of these techniques is without its limitations, however, and a need still exists

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for improved methods for obtaining mass spectra of involatile, heat-sensitive materials.

The problems of forming an ion vapor of involatile  
5 and heat-sensitive compounds become particularly acute  
when it is attempted to use a mass spectrometer to analyze  
the effluent of a liquid chromatograph. Liquid chromatographs  
are widely used to separate mixtures into their  
10 component compounds, and find particular application when  
one or more of the component compounds is too involatile  
to permit the mixture to be separated with a conventional  
gas chromatograph. Although mass spectrometers have been  
widely and successfully interfaced to gas chromatographs to  
15 permit mass spectra to be taken of compounds in the gaseous  
effluent from the chromatograph, efforts to interface  
liquid chromatographs to mass spectrometers have been  
less successful, in part because compounds eluted from the  
liquid chromatograph are frequently involatile and heat  
20 sensitive and thus not amenable to conversion into an ion  
vapor by conventional techniques. Moreover, the compounds  
to be analyzed from the liquid chromatograph are dissolved  
in a volatile solvent, which tends to reduce the ionization  
efficiency of the mass spectrometer even further with  
25 respect to the solute compounds of interest since solvent  
vapor is generally ionized along with the solute compounds  
and the solvent is typically in a much greater concentration  
than the solute compounds.

One attempt to interface a mass spectrometer to a  
30 liquid chromatograph is described in United States Patent  
No. 4,160,161 to Horton. Effluent from a liquid chromatograph  
is injected into an ion chamber maintained at a low  
pressure by means of a needle which projects into the  
chamber. The low pressure in the chamber, approximately  
35  $10^{-3}$  atmospheres, pulls the solvent and solute through

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the needle and sprays it into the chamber. A laser or other heat source may be utilized to prevent the effluent from freezing as it flows through the needle and to provide heat to the effluent in the ion chamber. The needle  
5 is maintained at a high voltage by a high voltage power supply so that droplets of spray carry a charge. The solvent evaporates in the low pressure environment, reducing the size of the charged droplets until ideally only the ions remain. In devices illustrated in Figures 1  
10 and 3 of the '161 patent, the ions travel in an unobstructed straight-line path through differentially pumped chambers and finally into an ion mass selector of the mass spectrometer system. In an apparatus illustrated in  
Figure 2, ions must be deflected electrostatically to pass  
15 through the differentially pumped chambers and into the ion mass selector.

The apparatus of the '161 patent has a serious drawback associated with the application of a high voltage to the needle projecting into the ion chamber. At the  
20 reduced pressure employed in the ion chamber approximately  $10^{-3}$  atmospheres, gases and vapors in the presence of high voltages tend to break down readily and become electrically conductive. As a result, uncontrolled electrical  
25 discharges are likely to occur in the ion chamber, leading to unstable and erratic behavior. A further problem would arise if the effluent solution from the liquid chromatograph were electrically conductive, as would be  
the case in reversed-phase liquid chromatography when  
30 aqueous buffers are used. If such conductive solutions were introduced into the needle maintained at a high voltage, substantial electrical current would flow through the solution between the needle and the liquid chromatograph, even if the conduit connecting them were made of  
35 an insulating material. Such a current flow could cause

electrolysis of the solution and other uncontrolled effects.

Disclosure of Invention

5

We have invented an improved ion vapor source and process which permits an ion vapor to be generated efficiently from a large class of liquid samples, including in many instances solutions of involatile and heat-sensitive compounds such as might be eluted from a liquid chromatograph, and which avoids the problems in the prior art noted above.

10

Broadly, the process of the invention concerns generating an aerosol from a liquid sample in which a fraction of the particles in the aerosol may be electrically charged. As used herein, the term "particle" encompasses liquid droplets and solid particles, but, consistent with conventional usage, does not encompass ions or molecules in a gaseous phase. The aerosol can be generated by metering the liquid into a capillary passageway and heating the walls of a length of the passageway sufficiently strongly to atomize the liquid to a mixture including vapor and particles. The process of the invention further includes the step of maintaining a vaporization surface, preferably located in a region maintained at a subatmospheric pressure, at a temperature above an impact-vaporization temperature of the particles. The process further includes the step of directing at least a fraction of the particles to impinge upon the vaporization surface. Upon colliding with the surface the particles are vaporized and an ion vapor formed. Electric charge to form the ions is preferably carried by the particles striking the vaporization surface. Alternatively, charge may be generated at the surface in the impact vaporization

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process in certain cases. If desired, vapor from the vaporization surface can be ionized using conventional chemical or electron impact ionization.

5                   Surprisingly, many involatile chemical compounds which decompose rather than vaporize when heated can be converted by preferred embodiments of the present invention into an ion vapor suitable for analysis by a mass spectrometer. The mass spectrum of an ion vapor so  
10 produced generally exhibits little evidence of pyrolytic decomposition and, moreover, generally exhibits relatively little of the ion fragmentation characteristic of mass spectra obtained using the conventional electron impact ionization technique. The process of the invention can  
15 therefore be termed a "soft" ionization technique.

When a mixture of aerosol and vapor is generated from a solution by strongly heating the walls of a length of a capillary passageway and metering the solution into  
20 the passageway, it is generally found that solutes which are less volatile than the solvent are preferentially contained in the particles of the aerosol. Furthermore, particularly when using polar solvents, it is found that particles of the aerosol are electrically charged, even  
25 when no electrical voltages are applied. If the capillary passageway is linear, the particles of the aerosol ejected from the passageway tend to form a beam with a relatively large component of the momentum of the particles directed along an axis of the passageway, as compared to components  
30 of momentum transverse to the axis. As a result, the beam of particles tends to be contained in a narrow cone about the axis of the passageway, which facilitates directing a substantial fraction of the particles ejected from the passageway against the vaporizer surface.  
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A preferred ion vapor source capable of carrying out the process of the invention on liquid samples for a mass spectrometer includes a housing attached to the mass spectrometer. The housing is generally vacuum tight with the interior of the housing defining a vacuum chamber. An evacuation port opens into the vacuum chamber and is connectable to a vacuum pump for maintaining the vacuum chamber at a subatmospheric pressure. It is preferred to maintain the pressure in the vacuum chamber in a range of from about 0.1 torr to about 10 torr. In addition, the housing has an inlet port and an ion-vapor discharge orifice which communicates between the vacuum chamber and an ion vapor inlet of the mass spectrometer.

The ion vapor source also includes an atomizing nozzle assembly which is secured to the inlet port of the housing to form a vacuum-tight seal. A passageway extends through the atomizing nozzle assembly for introducing a liquid sample into the vacuum chamber. A first end of the passageway defines a liquid sample inlet for receiving the liquid sample. For example, the nozzle assembly could be connected to a liquid chromatograph to permit liquid samples eluted from the chromatograph to flow into the liquid sample inlet of the nozzle assembly. A second end of the passageway which opens into the vacuum chamber defines a spray outlet for discharging an atomized spray of vapor and particles of the sample into the chamber. A nozzle heater is provided for heating at least a portion of the nozzle assembly sufficiently strongly to heat the liquid sample flowing in the passageway to atomize the sample. An electrical resistance heater or oxy-hydrogen torches capable of heating the atomizing nozzle assembly to incandescence are preferred nozzle heaters.

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The ion vapor source also includes a surface vaporizer for intercepting particles of sample for vaporization. The surface vaporizer includes a vaporizer surface located within the vacuum chamber in the vicinity of the ion-vapor discharge orifice. The vaporizer surface is positioned and oriented so that at least a fraction of the particles discharged from the spray outlet of the nozzle assembly are intercepted by the vaporizer surface. The vaporizer surface can be heated to an impact-vaporization temperature by a surface vaporizer heater such as an electrical-resistance heating element in thermal contact with the vaporizer surface. Particles of sample impinging upon the surface can be vaporized to form an ion vapor for introduction into the ion-vapor inlet of the mass spectrometer.

The ion vapor source of the present invention is particularly suited to interface a liquid chromatograph to a mass spectrometer. The effluent from a liquid chromatograph is typically a solution of a solute compound at a low concentration in a relatively volatile solvent. When such a solution is introduced into a mass spectrometer equipped with a preferred ion vapor source of the present invention, the mass spectrum obtained generally shows the solvent peaks to be orders of magnitude lower in intensity relative to the intensity of the solute peaks than would be expected on the basis of their relative mole fractions in the solution. The reduced solvent peak intensity arises in part because under preferred operating conditions roughly 95 percent of the solvent in the solution is vaporized before the particles of sample impinge upon the vaporizer surface, thereby concentrating the solution. Moreover, it appears in many cases that the electric charges on the particles and whatever additional charges are picked up at the vaporizer surface are preferentially carried by the solute molecules after vaporization on the vaporization surface.

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Certain solutions of compounds can be ionized both by embodiments of the present invention which involve no chemical or electron-impact ionization and by a conventional chemical ionization technique. Mass spectra of such a solution taken using the two ionization techniques permit the two techniques to be compared. Generally it is found that the total intensity of the peaks attributed to the solute is less by one or two orders of magnitude for spectra taken with the present invention as compared with spectra taken using chemical ionization. However, the total intensity of the solvent peaks is typically four or five orders of magnitude lower in intensity for spectra taken with the present invention as compared to spectra taken using chemical ionization. Thus in many cases the intensity of the solute ions over the solvent ion background can be increased with the present invention by two to four orders of magnitude relative to conventional chemical ionization.

Generally the overall sensitivity of a mass spectrometer equipped with an ion vapor source of the present invention depends upon the nature of the liquids analyzed. In the case of solutions, the nature of the solvent is a significant factor. Polar solvents such as water and methanol ordinarily provide the best results for embodiments of the invention which involve no chemical or electron-impact ionization. Dilute formic acid is particularly preferred as a polar solvent. Dilute formic acid is a suitable solvent for many compounds of biological interest and can be used in conventional liquid chromatography. Hexane, a nonpolar solvent, has not given satisfactory intensities when used with embodiments of the present invention which involve no electron impact or chemical ionization. Consequently, when using hexane

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as a solvent, it is preferred to employ a supplemental ionization technique, such as chemical ionization, subsequent to vaporization on the vaporizer surface.

5 Both positive and negative ions can be produced with embodiments of the present invention which employ a heated nozzle for atomization and involve no electron-impact or chemical ionization. Ordinarily, positive ions are formed more readily in such embodiments, so that  
10 positive ion spectra taken using the present invention are generally more intense than corresponding negative ion spectra. Charged particles of either polarity can be generated with the heated atomizing nozzle assembly of the preferred embodiment of the invention. The polarity  
15 depends at least in part on the nature of the liquid atomized, the temperature to which the nozzle is heated, and the rate of flow of the liquid through the heated zone.

20 Preferred ion vapor sources of the present invention can be inexpensive to manufacture relative to conventional ion sources used in mass spectrometry. No high-voltage source or electrostatic deflector is required to generate an ion vapor in accordance with preferred  
25 processes of the invention.

The ion vapor source of the present invention can operate at pressures as high as about one torr or even higher. In fact, in certain instances it has been  
30 observed that reducing the pressure surrounding the vaporization surface of an ion vapor source of the present invention to a high vacuum resulted in a drastically reduced ionization efficiency. Operation of the ion vapor

source at pressures as high as one torr or so is a significant advantage for liquid samples containing a relatively volatile solvent, since vacuum pumps with a capacity to pump away solvent vapor at a rate sufficient to maintain the interior of the source at a preferred pressure of one  
5 torr or so need not have a high-vacuum capability. Vacuum pumps having both a high-vacuum capability and a high pumping rate are expensive and bulky.

#### 10 Brief Description of the Drawings

The details of preferred embodiments of the invention will be described in connection with the accompanying drawings.

15 FIG. 1 is a side view in partial section of an ion vapor source of the present invention connected to a quadrupole mass spectrometer.

20 FIG. 2 is a side view in partial section of an atomizing nozzle assembly which employs electrical resistance heating.

25 FIG. 3 is a mass spectrum of adenosine 5'-monophosphate dissolved in dilute formic acid obtained with the mass spectrometer system of FIG. 1. The concentration of the phosphate was about 10 parts per million relative to the solvent.

#### 30 Best Mode for Carrying Out the Invention

Turning now to FIG. 1, an ion vapor source 2 is connected to a quadrupole mass spectrometer 4 to supply an ion vapor to the mass spectrometer for analysis. An  
35 atomizing nozzle assembly 5 includes a stainless steel

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capillary tube 6 having a capillary passageway 10 extending through it. The inside diameter of the capillary tube 6 could be about 0.15 mm, for example. The capillary tube 6 is electrically grounded. A liquid chromatograph 9 is connected to the capillary tube 6 for metering liquid effluent from the chromatograph into the capillary passageway 10. Four oxy-hydrogen torches 12 are disposed symmetrically around the capillary tube 6 at a discharge end portion 14 of the capillary tube. The discharge end portion of the capillary tube 6 is linear. A particle beam axis is defined by an axis of the linear discharge end portion 14. Each of the torches 12 has a burner tip 13 which is oriented to direct a flame from the torch against the capillary tube 6. A torch housing 16 surrounds the burner tips 13 of the torches 12. The torch housing 16 is provided with a vent 18 for venting the water vapor generated by the oxyhydrogen flames of the torches 12.

The passageway 10 of the capillary tube 6 opens into a spray input subchamber 20 which is defined by a generally vacuum-tight spray-input housing 22. The spray-input housing 22 has a first evacuation port 24 which permits the spray input subchamber 20 to be evacuated. The first evacuation port 24 is connected to a first vacuum pump (not shown) for maintaining the subchamber 20 at a subatmospheric pressure. A frustoconical skimmer 26 partitions the spray input subchamber 20 from a surface vaporization subchamber 30. The skimmer 26 has a pinhole collimator opening 28 passing through it which permits the spray input subchamber 20 to communicate with the surface vaporization subchamber 30. The collimator opening 28 is located on the particle beam axis.

The surface vaporization subchamber 30 is defined by the interior of a tubular surface vaporizer housing 32 which has a second evacuation port 34 which is connected to a second vacuum pump (not shown) for maintaining the

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interior of the surface vaporizer subchamber 30 at a subatmospheric pressure. An ion-vapor discharge orifice 36 passes through the surface vaporizer housing 32 and permits communication with the quadrupole mass spectrometer 4.

A surface vaporization probe 40 includes a support arm 42 and a surface-vaporizer probe tip 44. The probe tip 44 is made of nickel-plated copper and has a planar face which defines a vaporizer surface 46. The vaporizer surface 46 is positioned and oriented to intercept the particle beam axis. An electrically-resistive heating element 48 is located within the interior of the surface-vaporization probe 40 for heating the vaporizer surface 46 to temperatures ranging from ambient temperature up to about 350°C. If desired, an electron beam generator (not shown) could be positioned to direct an electron beam to a region close to the vaporizer surface 46 and the ion vapor discharge orifice 36 to permit conventional electron impact ionization and chemical ionization to be carried out in the ion vapor source 2.

The quadrupole mass spectrometer 4 is conventional and will therefore only be described briefly. Accelerating electrodes 50 are positioned close to the ion vapor discharge orifice 36 of the ion vapor source to accelerate ions in the ion vapor issuing from the discharge orifice. A partition 52 having a pinhole opening 54 is located adjacent to the accelerating electrodes 50 to form an ion beam. A pair of deflector electrodes 56 serves to bend the ion beam and direct it along a fourfold symmetry axis of four rod electrodes 58 of the quadrupole mass spectrometer 4. (Only two of the rod electrodes 58 are visible in FIG. 1). The rod electrodes 58 are connected to control circuitry (not shown)



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which provides the conventional DC and radio-frequency signals which enable quadrupole mass spectrometers to effect a "mass filtering" of an ion beam. Two beam-offset electrodes 60 and 62 and an ion multiplier 64 are positioned past a beam-exit end of the four rod electrodes 58. The beam-offset electrodes steer the mass-filtered ion beam leaving the four rod electrodes 58 into the ion multiplier 64 for detection. The interior of the mass spectrometer 4 is evacuated to a high vacuum through a first evacuation port 66. A region surrounding the accelerating electrodes 50 is evacuated to a high vacuum through a second evacuation port 68.

Turning now to FIG. 2, an electrically-heated nozzle assembly 100 includes an annular heat-transfer block 8 surrounding a stainless steel capillary tube 6 as discussed in connection with FIG. 1. The heat-transfer block 8 is made of copper and makes thermal contact with the capillary tube 6. An array of electrically-resistive heating elements 102 are disposed around the heat-transfer block 8, and are capable of heating the heat-transfer block 8 to temperatures of up to roughly 1000°C.

A preferred mode of operation of the ion-vapor source 2 of FIG. 1 will now be described. A solution of an involatile compound to be mass analyzed dissolved in a polar solvent such as water or methanol is metered into the capillary tube 6 and caused to flow towards the discharge end. Flow rates of from about 0.5 ml/min to about 1 ml/min are preferred for capillaries of the preferred dimensions set forth above. A length of the capillary tube 6 is heated to a temperature sufficient to atomize the solution by the oxy-hydrogen torches 12 of FIG. 1 or the electrically resistive heating elements 102 of FIG. 2. Heating the capillary tube 6 to incandescence,

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as high as 1000°C or higher, is generally preferred. Upon entering the capillary passageway 10 leading through the heated zone of the capillary tube 6, the solution is atomized and a mixture of vapor and an aerosol is ejected from the passageway into the spray input subchamber 20. It is believed that vaporization of the solvent protects the solute from pyrolysis in passing through the incandescent capillary tube 6. The particles of the aerosol tend to form a beam along the particle beam axis defined by the axis at the discharge end portion 14 of the capillary tube 6.

The pressure in the spray input subchamber 20 is maintained at about one torr by pumping with a vacuum pump connected to the first evacuation port 24. Solvent tends to evaporate, or sublime, as the case may be, from the aerosol particles in the reduced pressure environment of the spray input subchamber 20, thereby increasing the concentration of the involatile solute in the particles. Preferably only about 5 percent of the solvent relative to the original solution remains in the particles when the particles strike the vaporizer surface 46.

A fraction of particles ejected from the capillary passageway 10 of the heat-transfer block 8 pass through the collimator opening 28 of the skimmer 26 and into the surface vaporization subchamber 30. The surface vaporization subchamber 30 is maintained at a pressure of about 1 torr. The vaporizer surface 46 is heated to a temperature sufficient to vaporize the particles impacting the surface. Satisfactory operation has been achieved by maintaining the vaporization surface 46 at about 250°C. Particles passing through the collimator opening 26 strike the vaporizer surface 46 and are vaporized to form an ion vapor. It is believed that ordinarily the electric charge

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in the ion vapor is for the most part derived from charges carried by the particles from their formation at the heated zone of the capillary tube 6. However, additional charging may possibly take place upon impact vaporization at the vaporization surface 46. Typically a greater fraction of the solute molecules are ionized in the ion vapor than are the solvent molecules.

Ion vapor formed at the vaporization surface 46 passes through the ion-vapor discharge orifice 54 and enters the quadrupole mass spectrometer 4 for mass analysis.

The present invention has only recently been discovered and the various phenomena involved are not yet fully understood. It is believed tentatively that the extreme rapidity with which the minute particles of sample are heated upon striking the vaporizer surface may be a significant factor in explaining why involatile compounds which decompose upon being heated at more usual slow rates often yield an ion vapor in the present invention with little if any evidence of decomposition. In addition, the sudden vaporization of residual volatile solvent in the particles may tend to sweep involatile solute molecules into a gaseous phase.

#### Example

A solution of adenosine 5'-monophosphate (AMP) in a solvent of 0.2 molar formic acid was prepared by dissolving 0.1 mg of AMP in one milliliter of the solvent. AMP is a relatively involatile compound which is thermally labile.

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A liquid chromatograph with the column removed was connected to the capillary tube 6 of the ion-vapor source 2 of FIG. 1 to serve as an inlet system for metering samples into the ion vapor source. A sample of 20  $\mu$ l of the AMP solution was injected into the liquid chromatograph using 0.2 molar formic acid as the liquid phase. The flow rate was 0.5 ml/min. The heat-transfer block 8 was maintained at roughly 1000°C and the vaporizer surface 46 was heated to about 250°C. Both the spray input subchamber 20 and the surface vaporization subchamber 30 were maintained at a pressure of about one torr.

FIG. 3 presents the resulting mass spectrum. The spectrum was scanned from about 10 to about 600 amu in about 4 seconds. The most intense peak is of the protonated molecular ion of AMP. The protonated molecular ion of this compound was not observed when conventional chemical ionization was employed. A mass spectrum of AMP similar to the spectrum of FIG. 3 has been obtained by a field-desorption ionization technique.

The peaks below mass 100 in the mass spectrum of FIG. 3 are due to the solvent. Considering that the concentration of AMP in the sample was about 10 parts per million relative to the solvent, the ratio of the intensity of the ions derived from AMP to the intensity of the solvent ions is amazingly high.

It is not intended to limit the present invention to the specific embodiments described above. For example, the ion vapor source need not be attached to a mass analyzer. In this regard, the ion vapor source could be connected to an ion current meter and serve as a detector for a liquid chromatograph. Since satisfactory results are obtained with the spray input subchamber 20

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and the surface vaporization subchamber 30 maintained at about the same pressure, it is expected that the partition separating the two subchambers could be eliminated. An electron beam generator could be mounted in the apparatus of FIG. 1 to direct an electron beam into the surface vaporization subchamber along a direction mutually perpendicular to the particle beam axis and an axis defined by the support arm 42 of the vaporization probe 40. Such an electron beam generator could be used to initiate chemical ionization in vapor from the vaporization surface 46, and would be of particular advantage for solutions with nonpolar solvents such as hexane. It is recognized that these and other changes may be made in the apparatus and method specifically described herein without departing from the scope and teachings of the invention, and it is intended to encompass all other embodiments, alternatives, and modifications consistent with the present invention.

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Claims

1. An ion vapor source for obtaining an ion vapor from a liquid sample, the ion vapor source comprising:

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(a) a source housing having an interior defining an ionization chamber, an inlet port, and an ion-vapor discharge orifice;

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(b) an atomizing nozzle assembly secured to the inlet port of the source housing, the atomizing nozzle assembly having a passageway extending through it for introducing the sample into the ionization chamber, the passageway having a first end defining a liquid-sample inlet for receiving the liquid sample, and a second end opening into the ionization chamber, the second end of the passageway defining a spray outlet for discharging an aerosol including particles of the sample into the chamber, at least a portion of the walls of the passageway defining a sample heating surface;

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(c) a nozzle heater for heating the sample heating surface of the nozzle assembly to heat liquid passing through the passageway of the atomizing nozzle assembly;

30

(d) surface vaporizer means for intercepting particles of sample for vaporization, the surface vaporizer means having a vaporizer surface located within the ionization chamber in the vicinity of the ion vapor discharge orifice, the vaporizer surface being positioned and oriented such that at least a fraction of the

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particles discharged from the spray outlet of the nozzle assembly are intercepted by the vaporizer surface, and heat supply means for maintaining the vaporizer surface at an impact vaporization temperature such that particles of sample impinging upon the surface are vaporized to form an ion vapor for discharge from the ion-vapor discharge orifice.

2. The ion vapor source according to claim 1 in which the source housing is generally vacuum tight, the source housing having an evacuation port connectable to a vacuum pump for maintaining the ionization chamber at a pressure in the range of from about 0.1 torr to about 10 torr.

3. The ion vapor source according to claim 2 in which the heat supply means of the surface vaporizer means includes an electrical resistance heating element in a heat-transfer relationship to the vaporizer surface, the heating element being capable of maintaining the vaporizer surface at a temperature of at least about 350°C.

4. The ion vapor source according to claim 3 in which the atomizing nozzle assembly includes a metal capillary tube having a capillary channel extending through it to define the passageway of the nozzle assembly, the capillary tube being secured to the source housing in a vacuum-tight manner with the capillary channel of the capillary tube communicating with the ionization chamber through the inlet port of the housing; and

in which the atomizing heater means is adapted to heat at least a portion of the capillary tube to incandescence.

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5. The ion vapor source according to claim 4 in which the atomizing heater means includes a torch positioned and oriented so that in operation it directs a flame against the capillary tube block.

5

6. The ion vapor source according to claim 5 in which the torch is an oxy-hydrogen torch.

7. The ion vapor source according to claim 4 in  
10 which:

the capillary tube is made of stainless steel; and

15

the atomizing heater means includes a plurality of oxy-hydrogen torches disposed generally symmetrically around the capillary tube, each oxy-hydrogen torch being positioned and oriented so that in operation it directs a flame  
20 against the capillary tube.

20

8. The ion vapor source according to claim 4 in which the atomizing heater means includes an electrical-resistance heating element in a heat transfer relationship  
25 to the capillary tube.

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9. The ion vapor source according to claim 2  
in which

5 the source housing includes a vaporizer-  
probe port opening into the ionization chamber,  
and

the surface-vaporizer means includes:

10 (d.1) a vaporizer probe extending through  
the vaporizer probe port of the source  
housing and into the ionization chamber,  
the vaporizer probe being joined to the  
housing in a vacuum-tight manner, the  
15 vaporizer probe comprising

(i) a hollow support arm, and

20 (ii) a surface-vaporizer end cap joined in  
a vacuum-tight manner to an end of the  
support arm, the end cap extending into  
the ionization chamber and having a generally  
planar face defining the vaporizer surface,  
the support arm being positioned and  
25 oriented to locate the vaporizer surface in  
the vicinity of to the ion-vapor discharge  
orifice and facing in a direction such that  
in operation at least a fraction of the  
particles discharged from the spray outlet  
30 of the nozzle assembly are intercepted by  
the vaporizer surface; and

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(d.2) an electrical-resistance heating element located within the interior of the vaporizer probe in a heat-transfer relationship with the end cap for heating the vaporizer surface.

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10. The ion vapor source according to claim 9 in which the vaporizer surface is composed of nickel.

11. The ion vapor source according to claim 2 further comprising:

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(e) a collimator partition located within the ionization chamber, the collimator partition dividing the ionization chamber into a spray input subchamber and a surface vaporization subchamber, the spray outlet of the atomizing nozzle assembly communicating with the spray input subchamber, the ion vapor discharge orifice communicating with the surface vaporization subchamber, the vaporizer surface being located in the surface vaporization subchamber, the collimator partition having a collimator opening passing through it, the collimator opening being located along a straight-line path defined between the spray outlet of the atomizing nozzle assembly and a target point on the vaporizer surface so that particles discharged from the spray outlet passing through the collimator opening are moving in a direction to impinge upon the vaporizer surface.

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12. The ion vapor source according to claim 11 in which:

5 the collimator partition is secured to the source housing in a vacuum tight manner so that the spray input subchamber communicates with the surface vaporization subchamber substantially only through the collimator opening;

10 the evacuation port opens into the spray input subchamber for maintaining the spray input subchamber at a subatmospheric pressure; and

15 the source housing has an auxiliary evacuation port which opens into the surface vaporization subchamber, the auxiliary evacuation port being connectable to an auxiliary vacuum pump for maintaining the surface vaporization subchamber at  
20 a pressure in the range of from about 0.1 torr to about 10 torr.

13. The ion vapor source according to claim 12 in which the collimator partition at the collimator  
25 opening is shaped to form a frustoconical skimmer, the skimmer being generally circularly symmetric with a symmetry axis generally coinciding with the straight-line path defined between the spray outlet of the nozzle assembly and the target point of the vaporizer surface, a  
30 narrow end of the frustoconical skimmer facing the spray outlet of the nozzle assembly.

14. The ion vapor source according to claim 2 in which the atomizer nozzle assembly is electrically grounded.

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15. The ion vapor source according to claim 2 further comprising:

5 (e) an electron beam generator positioned and oriented to direct an electron beam into the ionization chamber in the vicinity of the vaporizer surface to permit vapor from the vaporization surface to be ionized by electron impact or chemical ionization.

10 16. A mass spectrometer for mass analyzing liquid samples comprising:

15 (a) a mass spectrometer having an ion vapor inlet for receiving ion vapor for mass analysis; and

20 (b) an ion-vapor source for obtaining an ion vapor from a liquid sample, the ion vapor source comprising:

25 (b.1) a source housing attached to the mass spectrometer, the source housing having an interior defining an ionization chamber, an inlet port, and an ion-vapor discharge orifice communicating between the vacuum chamber and the ion vapor inlet of the mass spectrometer;

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(b.2) an atomizing nozzle assembly secured to the inlet port of the source housing, the atomizing nozzle assembly having a passageway extending through it for introducing the sample into the ionization chamber, the passageway having a first end defining a liquid-sample inlet for receiving the liquid sample, and a second end opening into the ionization chamber, the second end of the passageway defining a spray outlet for discharging an atomized spray of vapor and particles of the sample into the chamber at least a portion of the walls of the passageway defining a sample heating surface;

(b.3) a nozzle heater for heating the sample heating surface of the nozzle assembly to heat liquid passing through the passageway of the atomizing nozzle assembly;

(b.4) surface vaporizer means for intercepting particles of sample for vaporization, the surface vaporizer means having a vaporizer surface located within the ionization chamber in the vicinity of the ion vapor discharge orifice, the vaporizer surface being positioned and oriented such that at least a fraction of the particles discharged from the spray outlet of the nozzle assembly are intercepted by the vaporizer surface, and heat supply means for maintaining the vaporizer surface at an impact vaporization temperature such that particles of sample impinging upon the surface are vaporized to form an ion vapor

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for discharge from the ion-vapor discharge orifice into the ion vapor inlet of the mass spectrometer for mass analysis.

5           17. The mass spectrometer according to claim 16  
in which:

10           the source housing of the ion vapor source is generally vacuum tight, the source having an evacuation port connectable to a vacuum pump for maintaining the ionization chamber at a pressure in the range from about 0.1 torr to about 10 torr;

15           the heat supply means of the surface vaporizer includes an electrical resistance heating element in a heat-transfer relationship to the vaporizer surface; and

20           the atomizing nozzle assembly includes a metal capillary tube having a capillary channel extending through it to define the passageway of the nozzle assembly; and the capillary tube being secured to the source housing in a vacuum-tight manner with the capillary channel of the  
25           capillary tube communicating with the ionization chamber through the inlet port of the housing; and

30           in which the atomizing heater means is adapted to heat at least a portion of the capillary tube to incandescence.

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18. A liquid chromatograph/mass spectrometer system comprising:

5 (a) a liquid chromatograph having a sample outlet for discharging effluent from the liquid chromatograph;

10 (b) a mass spectrometer having an ion vapor inlet for receiving ion vapor for mass analysis; and

(c) an ion vapor source for interfacing the liquid chromatograph to the mass spectrometer, the ion vapor source comprising:

15 (c.1) a source housing attached to the mass spectrometer, the source housing having an interior defining an ionization chamber, an inlet port, and an ion-vapor discharge orifice communicating between the ionization chamber  
20 and the ion vapor inlet of the mass spectrometer;

25 (c.2) an atomizing nozzle assembly secured to the inlet port of the source housing, the atomizing nozzle assembly having a passageway extending through it for introducing the sample into the ionization chamber, the passageway having a first end communicating with  
30 the sample outlet of the liquid chromatograph for receiving liquid effluent from the chromatograph, and a second end opening into the ionization chamber, the second end of the passageway defining a spray outlet for dis-  
35 charging an aerosol including particles of the effluent into the chamber, at least a portion

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of the walls of the passageway defining  
a sample heating surface;

5 (c.3) a nozzle heater for heating the  
sample heating surface of the nozzle assembly  
to heat the effluent passing through the  
passageway of the atomizing nozzle assembly;  
and

10 (c.4) surface vaporizer means for inter-  
cepting particles of effluent for vaporization,  
the surface vaporizer means having a vaporizer  
surface located within the ionization chamber  
in the vicinity of the ion vapor discharge  
15 orifice, the vaporizer surface being posi-  
tioned and oriented such that at least a  
fraction of the particles discharged from the  
spray outlet of the nozzle assembly are  
intercepted by the vaporizer surface, and heat  
20 supply means for maintaining the vaporizer  
surface at an impact-vaporization temperature  
such that particles of effluent impinging upon  
the surface are vaporized to form an ion vapor  
for discharge from the ion-vapor discharge  
25 orifice into the ion vapor inlet of the mass  
spectrometer for mass analysis.

19. The liquid chromatograph/mass spectrometer  
system according to claim 18 in which:

30 the source housing is generally vacuum tight,  
the source housing having an evacuation port connectable to  
a vacuum pump for maintaining the ionization chamber at a  
pressure in the range of from about 0.1 torr to about 10  
35 torr;



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the heat supply means of the surface vaporizer includes an electrical resistance heating element in a heat-transfer relationship to the vaporizer surface; and

5

the atomizing nozzle assembly includes a metal capillary tube having a capillary channel extending through it to define the passageway of the nozzle assembly, a first end of the capillary tube being connected to the sample outlet of the liquid chromatograph, the capillary tube being secured to the source housing in a vacuum-tight manner with the capillary channels of the capillary tube communicating with the ionization chamber through the inlet port of the housing; and

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in which the atomizing heater means is adapted to heat at least a portion of the capillary tube to incandescence.

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20. A detector for a liquid chromatograph or the like, comprising:

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(a) an ion vapor source for obtaining an ion vapor from liquid effluent from the liquid chromatograph, the ion vapor source comprising:

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(a.1) a source housing having an interior defining an ionization chamber, an inlet port, and an ion-vapor discharge orifice;

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(a.2) an atomizing nozzle assembly secured to the inlet port of the source housing, the atomizing nozzle assembly having a passageway extending through it for introducing the sample into the ionization chamber, the passageway having a first end defining a liquid-sample inlet for receiving liquid effluent from the liquid chromatograph, and a second end opening into the ionization chamber, the second end of the passageway defining a spray outlet for discharging an aerosol including particles of the effluent into the chamber, at least a portion of the walls of the passageway defining a sample heating surface;

(a.3) a nozzle heater for heating the sample heating surface of the nozzle assembly to heat the effluent passing through the atomizing nozzle assembly; and

(a.4) surface vaporizer means for intercepting particles of sample for vaporization, the surface vaporizer means having a vaporizer surface located within the ionization chamber in the vicinity of the ion vapor discharge orifice, the vaporizer surface being positioned and oriented such that at least a fraction of the particles discharged from the spray outlet of the nozzle assembly are intercepted by the vaporizer surface, and heat supply means for maintaining the vaporizer surface at an impact-vaporization temperature such that particles of sample impinging upon the surface are vaporized to form an ion

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vapor for discharge from the ion-vapor discharge orifice; and

5 (b) an ion-current meter for measuring the magnitude of an ion current, the ion-current meter having an ion vapor inlet and a current magnitude display, the ion vapor inlet being connected to the ion vapor discharge orifice of the ion vapor source for receiving ion vapor  
10 discharged from the ion vapor source.

21. The detector according to claim 20 in which:

15 the source housing is generally vacuum tight, the source housing having an evacuation port connectable to a vacuum pump for maintaining the ionization chamber at a pressure in the range of from about 0.1 torr to about 10 torr;

20 the heat supply means of the surface vaporizer means includes an electrical resistance heating element in a heat-transfer relationship to the vaporizer surface;

25 the atomizing nozzle assembly includes a metal capillary tube having a capillary channel extending through it to define the passageway of the nozzle assembly, a first end of the capillary tube being connectable to the sample outlet of the liquid chromatograph, the capillary tube  
30 being secured to the source housing in a vacuum-tight manner with the capillary bore of the heat-transfer block communicating with the ionization chamber through the inlet port of the housing; and

35 in which the atomizing heater means is adapted to heat at least a portion of the capillary tube to incandescence.

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22. A process of generating an ion vapor from a sample of liquid solution, the solution including a solute and a polar solvent, the process comprising the steps of:

5 (a) metering the solution into a first end of a capillary passageway;

10 (b) heating walls of a length of the passageway to incandescence to atomize the solution, the rate at which the solution is introduced into the passageway and the temperature of the walls being selected so that a mixture of vapor and particles from the solution are discharged from a second end of the passageway, at least a  
15 fraction of the particles being electrically charged;

20 (c) maintaining a substantially enclosed region at a subatmospheric pressure by evacuating the region with a vacuum pump;

25 (d) introducing at least a fraction of the vapor and particles discharged from the capillary passageway into the subatmospheric-pressure region to pump away a portion of the vapor with the vacuum pump;

30 (e) heating a vaporization surface to a temperature above an impact vaporization temperature of the particles at the subatmospheric pressure; and

35 (f) directing at least a fraction of the charged particles in the subatmospheric-pressure region to impinge upon the heated vaporization surface to be vaporized to form the ion vapor.

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22. The process according to claim 21 in which the pressure in the subatmospheric-pressure region is maintained at roughly 1 torr.

5           23. The process according to claim 22 in which a length of the capillary passageway passes through a copper heat-transfer block, and in which the step (b) of heating the walls of a length of the passageway includes the step of heating the heat-transfer block to a temperature of  
10 roughly 1000°C.

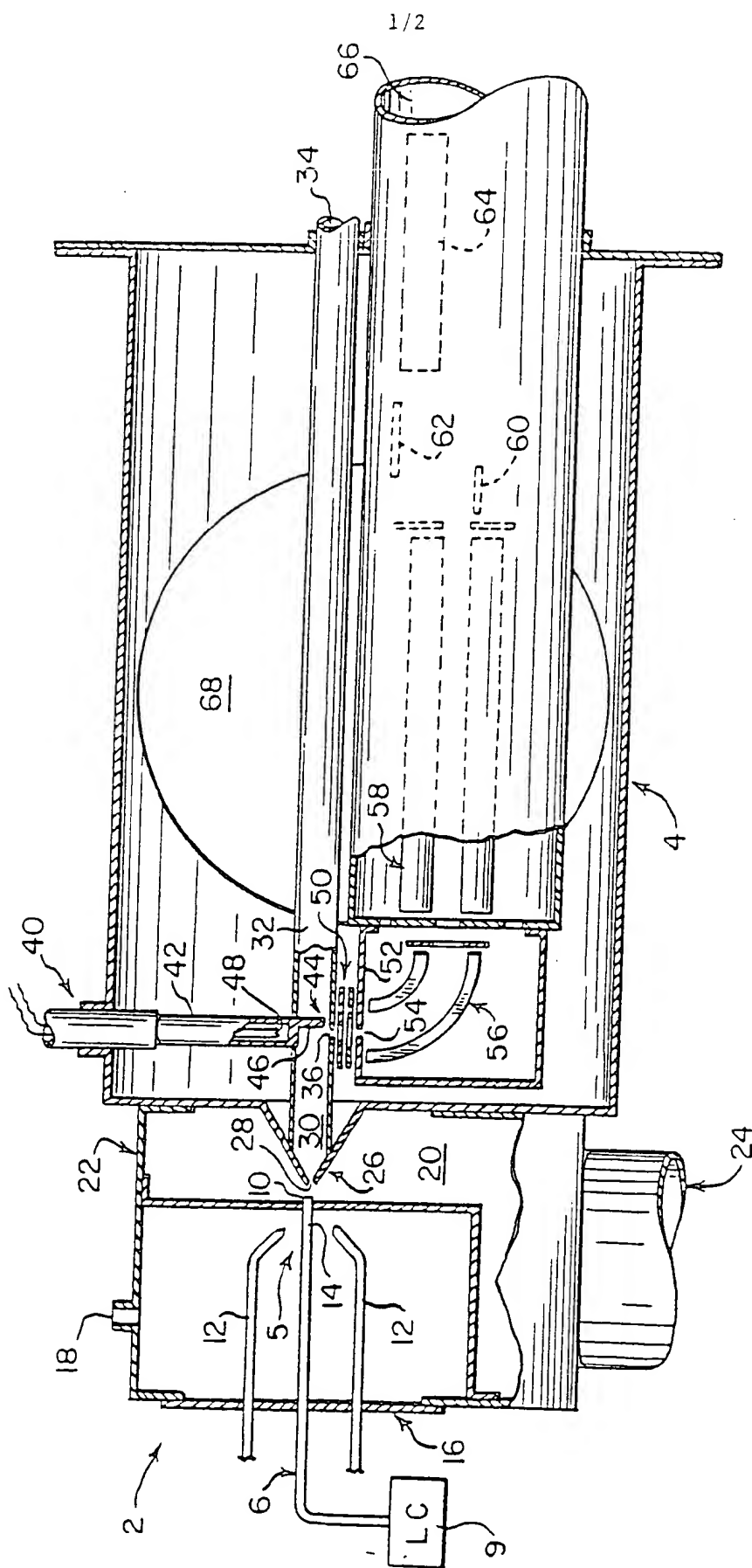
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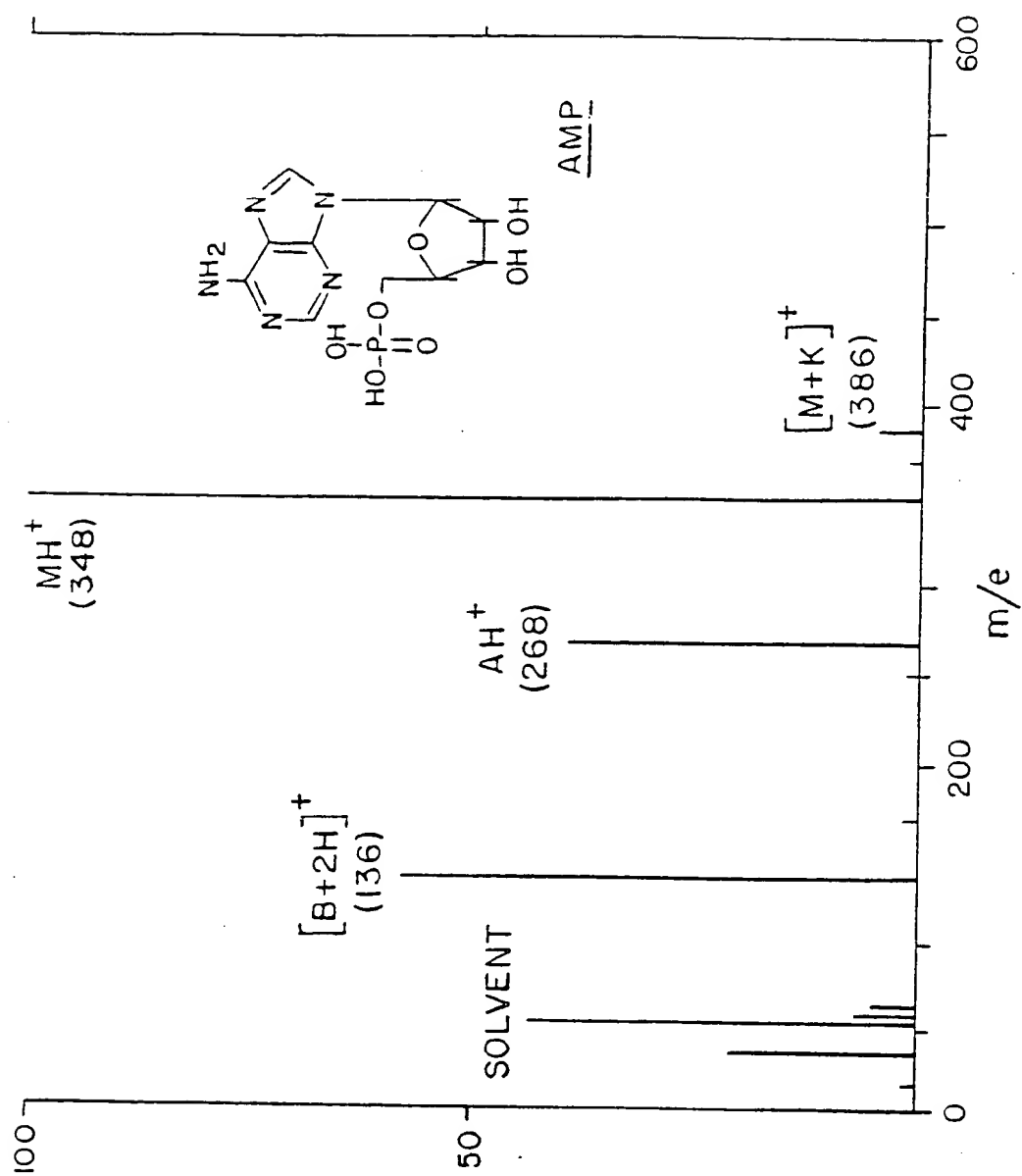


FIG. 3

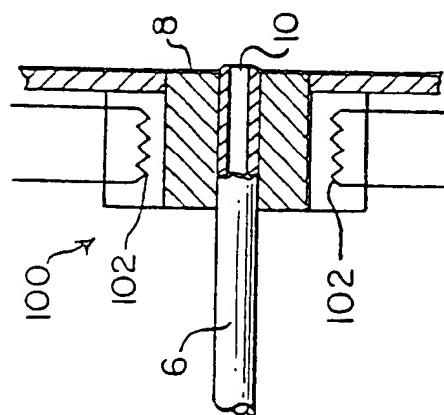


FIG. 2

# INTERNATIONAL SEARCH REPORT

International Application No. PCT/US81/00693

## I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all) <sup>1</sup>

According to International Patent Classification (IPC) or to both National Classification and IPC

INT. CL. <sup>3</sup> H01J 49/28

US. CL. 250/281

## II. FIELDS SEARCHED

Minimum Documentation Searched <sup>4</sup>

Classification System	Classification Symbols
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U.S.

250/281, 250/423, 250/425, 250/288  
73/61.3, 73/61.1C

Documentation Searched other than Minimum Documentation  
to the extent that such Documents are included in the Fields Searched <sup>6</sup>

## III. DOCUMENTS CONSIDERED TO BE RELEVANT <sup>14</sup>

Category <sup>8</sup>	Citation of Document, <sup>16</sup> with indication, where appropriate, of the relevant passages <sup>17</sup>	Relevant to Claim No. <sup>18</sup>
X, T	N, ANALYTICAL CHEMISTRY, VOL. 52, No. 11, BLAKLEY et al: LIQUID CHROMATOGRAPH-MASS SPECTROMETER FOR ANALYSIS OF NONVOLATILE SAMPLES page 1636-1641, issued September, 1980	
A,	US, A, 4,160,161, Published 3 July 1979, HORTON	
A	US, A, 4,055,987, Published 1 November 1977, McFADDEN	
A	US, A, 4,144,451, Published 3 March 1979, KAMBARA	
A	US, A, 2,621,296, Published 9 December 1952, THOMPSON	
A	US, A, 3,336,475, Published 15 August 1967, KILPATRICK	

\* Special categories of cited documents: <sup>15</sup>

"A" document defining the general state of the art

"E" earlier document but published on or after the international filing date

"L" document cited for special reason other than those referred to in the other categories

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but on or after the priority date claimed

"T" later document published on or after the international filing date or priority date and not in conflict with the application, but cited to understand the principle or theory underlying the invention

"X" document of particular relevance

## IV. CERTIFICATION

Date of the Actual Completion of the International Search <sup>1</sup>

11 August, 1981

Date of Mailing of this International Search Report <sup>2</sup>

18 AUG 1981

International Searching Authority <sup>3</sup>

ISA/US

Signature of Authorized Officer <sup>10</sup>

H. A. Dixon